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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/043,933	03/30/1998	JEAN-MARC BALLOUL	017753-094	7553

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/23/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/043,933	Applicant(s) BALLOUL ET AL.	
	Examiner Shanon A. Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-20,38,40,42-47,49,52-63,65 and 68-78* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,40,42-47,49,52-63,65 and 68-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant has cancelled claims 39, 41, 48, 50, 51, 64, 66, and 67 and amended claims 38, 40, 47, 49, 52, 53, 55, 63, 68, 69, 71, and 74. Claims 10-20 are also pending, but are withdrawn from consideration due to a non-elected invention. Claims 38, 40, 42-47, 49, 52-63, 65, 68-78 are under consideration.

Priority

Applicant argues on pages 11 and 12 of amendment I that Stanley et al. in WO 96/29091 is not available under U.S.C. §102(a) because Stanley et al. was published September 26, 1996 and the claim to foreign priority in the instant application is French application number 96 09584 filed on July 30, 1996.

Although the Examiner has acknowledged the claim to foreign priority, applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15. Therefore, the teachings of Stanley et al. in WO 96/29091 are available under U.S.C. §102(a) as prior art.

Claim Objections

Claims 56, 57 and 72, 73 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claims 55 and 71, respectively. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 55 and 71 state that E6 has amino acids 111-115 deleted and E7 has amino acids 21-26 deleted. Therefore, the limitations recited in claims 56, 57 and 72, 73 are not further limiting.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 38, 40, 42-47, 49, 52-63, 65, 68-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 is drawn to pharmaceutical composition comprising at least one early polypeptide and at least one late polypeptide from the papillomavirus, with the exception of a DNA sequence encoding E7 and L2. Subsequent dependent claims 40 and 42 state that the early polypeptides E6 and/or E7 and L1 and/or/L2. In addition, independent claims 47 and 63 state that the composition includes one late and one early protein from the papillomavirus, which would include the combination E7 and L2. Therefore, the compositions are contradictory in the claims and it is unclear what Applicant intends. This rejection also affects dependent claims 40, 42-47, 49, 52-63, 65, 68-78.

Claim 68 recites the limitation "interleukin-2" in line 2. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38, 40, 42-47 and 63, 65, 68-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The added material which is not supported by the original disclosure is as follows: claim 38 is now directed to at least one early polypeptide and one late polypeptide from the papillomavirus with the specific exception of E7 and L2 combination. This negative limitation cannot be found in the original disclosure. Although recent evidence has developed pointing to a lack of enablement for some of the embodiments in the instant application, an exclusion of specific elements (E7 and L2), is not supported in the original claims or specification. Therefore, Applicant cannot add this exclusion to these particular embodiments. This rejection also affects claims 40, 42-47.

Claim 63 recites immunostimulatory molecule IL-1. The Examiner is unable to find support for this new limitation in the original specification or claims. This rejection also affects claims 65, 68-78.

Applicant is requested cancel the new matter indicated for claims 38, 40, 42-47 and to point to support for IL-1 in the specification or cancel the new matter indicated for claims 63, 65, 68-78.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 38, 40, 42-46 are rejected under 35 U.S.C. 102(a) as anticipated by Stanley et al. (WO 96/29091) for reasons of record.

Applicant states that the composition of Stanley et al. (WO 96/29091) comprises at least one papillomavirus polypeptide or a substantial part of one of the proteins recited on page 4, lines 33-38, which includes up to 80 possible combinations. Applicant has also supplied a partial summary of the combinations on page 10 of the response, which includes E2+L1 and E2+L2. It is noted that these combinations of Stanley et al. anticipate instant claim limitations reciting a pharmaceutical composition comprising at least one polypeptide from the early and late region of a human papillomavirus.

Applicant argues that Stanley et al. does not consider injecting papillomavirus polypeptides in the absence of IL-12 and does not does not provide sufficient guidance when the skilled artisan uses other immunostimulatory molecules.

In response, since applicant has amended the claims to specifically recite immunostimulatory molecules not recited by Stanley et al., arguments presented for lack of guidance in using other immunostimulatory molecules are moot. With respect to Stanley et al. not considering an injection without IL-12, the instant composition of claim 38 recites "comprising" in line 2, which does not exclude other components such as IL-12.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38, 40, 42-47, 49, 52-54, 58-63, 65, 68-70, 74-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galloway (Infectious Agents and Disease. 1994; 3: 187-193), Hines et al. (Obstetrics and Gynecology. 1995; 86 (5): 860-866), and Gajewski (Journal of Immunology. 1996; 156: 465-472) for reasons of record.

Applicant states on page 15 and 16 that Galloway teaches that the late proteins confer immunity and that the early proteins retard the development of tumors, and Galloway further teaches that a composition comprising the L2+E7 combination. It is noted that this combination anticipates claim limitations in the claims drawn to selecting at least one early and one late polypeptide.

Applicant reiterates that this particular combination is excluded from the amended claims. Applicant also draws attention to the fact that the claims now incorporate expression from independent expression control elements. Applicant also argues that Galloway does not teach using immunostimulatory molecules.

As stated above, the specification does not convey this exclusion and it is considered to be new matter. In addition, one of ordinary skill in the art at the time the invention was made would have been motivated express the proteins from independent control elements in order to control transcription and subsequently, the amount of protein expressed in the cell. It was previously noted in the previous Office action that Galloway does not teach using immunostimulatory molecules, which is why the reference was paired with another that does teach those elements (i.e. Hines et al. and Gajewski).

With respect to Hines et al., applicant argues that the reference does not teach injecting IL-2 into a patient together with HPV polypeptides to enhance the protective effect conferred by the papillomavirus pepides.

Hines et al. is used to demonstrate the natural stimulatory capabilities of IL-2 to activate cytotoxic T cells to combat HPV anti-tumor responses. One of ordinary skill in the art at the time the invention was made would have been motivated to administer IL-2, a natural immunostimulator, in combination with therapeutic HPV early proteins and the preventative HPV late proteins taught by Galloway and Hines et al. to specifically activate the immune system to the administered proteins.

Applicant argues that Gajewski does not teach administering B7.1 with an HPV peptide to provide protection against HPV infection.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As summarized by applicant on page 18, Gajewski teaches that B7.1 transfected tumor cells stimulate proliferation of CD4+ and CD8+ cells and direct stimulation of B7.1 induces CTLs to produce their own IL-2, and that this method provides an immunization approach for cancer patients. One of ordinary skill in the art at the time the invention was made would have been motivated to administer B7.1 to immunize cancer patients (i.e. patients with HPV-cervical carcinoma) to induce the production of IL-2 and to specifically stimulate CD4+ and CD8+ cells against the therapeutic early proteins and the preventative late proteins taught by Galloway and Hines et al.

Claims 55-57 and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galloway, Hines et al., and Gajewski et al. as applied to claims 47, 49, 52-54, 58-63, 65, 68-70, 74-78 above, and further in view of Munger et al. (The EMBO Journal. 1989; 8: 4099-4105) and Crook et al. (Cell. 1991; 67: 547-556) for reasons of record.

Since the combination of Galloway, Hines et al., and Gajewski render the invention prima facie obvious to one of ordinary skill in the art at the time the invention was made, the rejection under the teachings of Crook et al. and Munger et al. is maintained for reasons of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SAF

Shanon Foley/SAF
November 8, 2001

James C. Housel

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